

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of: Jaya Pathak, et al.	Examiner: Lin, James
Serial No. 10/631,228	Art Unit: 1792
Filed: July 31, 2003	Confirmation No.: 1730
Title: Method and System of Purifying Polymers For Use With Implantable Medical Devices	

**Mail Stop Appeal Brief-Patents**

Commissioner for Patents

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**APPEAL BRIEF**

Sir or Madam:

On January 26, 2009, Applicants appealed to the Board of Patent Appeals and Interferences from the final rejection of claims 1, 3-5, 8-10, 13, 16-18, 23-29, and 31-37. The following is Applicants' Appeal Brief submitted pursuant to 37 C.F.R. § 41.37.

**I. REAL PARTY IN INTEREST**

The real party in interest with regard to this appeal is Abbott Cardiovascular Systems, Inc., with its primary place of business at 3200 Lakeside Drive, Santa Clara, California 95054. The assignment to Advanced Cardiovascular Systems, Inc., was recorded in the United States Patent and Trademark Office on November 14, 2003, in Reel 014695, Frame 0908. Abbott Cardiovascular Systems, Inc. purchased the vascular device division and all relevant intellectual property including the instant application of Advanced Cardiovascular Systems, Inc. (Guidant Corporation) in April 2006.

**II. RELATED APPEALS AND INTERFERENCES**

Applicants, applicants' assignee, and their counsel are not aware of any related appeals or interferences which would affect, be affected by, or have a bearing on the instant appeal.

### **III. STATUS OF CLAIMS**

Claims 1, 3-5, 8-10, 13, 16-18, 23-29, and 31-37 have been rejected by the Examiner (and the rejections thereof are being the basis of this appeal).

Claims 7, 11, 12, 14, and 19-22 have been withdrawn from consideration.

Claims 2, 6, 15 and 30 have been canceled.

### **IV. STATUS OF AMENDMENTS**

All amendments have been accepted into the record. A Notice of Appeal was filed on January 26, 2009.

### **V. SUMMARY OF CLAIMED SUBJECT MATTER**

The appealed application contains four independent claims, the support for which can be found in the specification as follows: Independent claim 1<sup>1</sup> is directed to a method of manufacturing a medical device. The method includes purifying a polymer for use with the medical device (page 5, lines 4-5). A fluid is introduced into a mixing apparatus and mixed with the polymer. (*Id.* at 8-9). As the fluid is mixed with the polymer, the

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<sup>1</sup> 1. A method of manufacturing an implantable medical device, comprising:  
purifying a polymer by:  
introducing the polymer into a mixing apparatus;  
introducing a fluid into the mixing apparatus;  
mixing the fluid with the polymer;  
removing at least a volume of the fluid from the mixing apparatus such that an impurity is completely or at least partially removed with the fluid; and  
collecting the polymer after removal of the impurity; and  
coating an implantable medical device with the purified polymer, or fabricating the implantable medical device with the purified polymer;  
wherein the fluid is of a type to physically entrap the impurity without dissolving the impurity.

fluid acts to remove impurities from the polymer (*Id.* at 9-10). After the impurities have been removed from the polymer by the fluid, the fluid containing the impurity is removed from the mixing apparatus and the purified polymer is collected. (*Id.* at 10-12). After the polymer has been purified, the polymer can be applied to a stent to form a coating (page 15, lines 12-13). The device can be made partially or completely from a purified bioabsorbable or biostable polymer (page 14, lines 17-20). The fluid is of the type to physically entrap the impurity without dissolving the impurity (page 8, lines 6-10).

Claim 13<sup>2</sup> presented in the response of August 25, 2008 includes an error. The limitation of “removing the impurity with the fluid” was deleted in the response dated November 27, 2007. When duplicating claim 13 in the response of August 25, 2008, Appellants inadvertently forgot to remove this line. The claim no longer includes “removing the impurity with the fluid.” Appellants are assuming that the Examiner did not notice this inadvertent error, as no objection was raised in the Final Office Action of November 25, 2008. The correct version is duplicated in footnote 2 and accompanying appendix.

Claim 13 is directed to a method of manufacturing a coating for an implantable medical device. The method includes purifying a polymer for use with the medical device (page 5, lines 4-5). A fluid is introduced into an extruder, such as a single screw extruder, intermeshing co-rotating and counter-rotating twin-screw extruder, or other multiple screw masticating extruder (page 10, lines 8-10). The fluid is mixed in the polymer and acts to remove impurities from the polymer (page 5, lines 9-10). After the

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<sup>2</sup> 13. A method of manufacturing a coating for an implantable medical device, comprising:

- (a) purifying a thermoplastic polymer, the purifying including introducing the polymer into an extruder, introducing a fluid into the extruder, mixing the fluid with the polymer, removing at least a portion of the fluid and an impurity from the extruder, and collecting the polymer after removal of the impurity; and
- (b) applying a composition to an implantable medical device, the composition including the purified polymer, a solvent and optionally a therapeutic agent; wherein the fluid is of a type to physically entrap the impurity without dissolving the impurity.

impurities have been removed from the polymer by the fluid, the fluid containing the impurity is removed from the extruder and the purified polymer is collected. (*Id.* at 10-12). After the polymer has been purified, the polymer is applied to a stent by dissolving the polymer in a coating solvent, or a mixture of solvents, and applying the resulting solution on the stent (page 16, lines 1-5). The purified polymer may also be combined with an active agent. (*Id.* at 15). The fluid is of the type to physically entrap the impurity without dissolving the impurity (page 8, lines 6-10).

Claim 23<sup>3</sup> is directed to a method of manufacturing a medical device. The method includes purifying a polymer for use with the medical device (page 5, lines 4-5). A fluid is introduced into a mixing apparatus and mixed with the polymer. (*Id.* at 8-9). The fluid may include FLUX REMOVER AMS, dimethyl acetamide, dimethyl formamide, dimethyl sulfoxide, and combinations thereof (page 9, lines 4-6). As the fluid is mixed with the polymer, the fluid acts to remove impurities from the polymer (page 5, lines 9-10). After the impurities have been removed from the polymer by the fluid, the fluid containing the impurity is removed from the mixing apparatus and the purified polymer is collected (*Id.* at 10-12). After the polymer has been purified, the polymer is applied to a stent to form a coating (page 15, lines 12-13).

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<sup>3</sup> 23. A method of manufacturing an implantable medical device, comprising: purifying a polymer by:

- introducing the polymer into a mixing apparatus;
- introducing a fluid into the mixing apparatus, the fluid selected from the group consisting of FLUX REMOVER AMS, dimethyl acetamide, dimethyl formamide, dimethyl sulfoxide, and combinations thereof;
- mixing the fluid with the polymer;
- removing at least a volume of the fluid from the mixing apparatus such that an impurity is completely or at least partially removed with the fluid; and
- collecting the polymer after removal of the impurity; and
- coating an implantable medical device with the purified polymer.

Claim 31<sup>4</sup> is directed to a method of manufacturing a medical device. The method includes purifying a polymer for use with the medical device (page 5, lines 4-5). A first fluid is introduced into a mixing apparatus and mixed with the polymer where the first fluid acts as a solvent for an impurity (page 8, lines 11-12). As the fluid is mixed with the polymer, the fluid acts to remove impurities from the polymer. After the impurities have been removed from the polymer by the fluid, the fluid containing the impurity is removed from the mixing apparatus (page 5, lines 9-12). A second fluid is introduced into the mixing apparatus and acts as a non-solvent for the impurity (page 8, lines 18-19). The second fluid is mixed with the polymer to remove the impurity. After the polymer has been purified, the polymer is applied to a stent to form a coating (page 15, lines 12-13). The device can be made partially or completely from a purified bioabsorbable or biostable polymer (page 14, lines 17-20). Two different fluids may be used to extract an impurity (page 8, lines 11-12).

## **VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL**

The grounds of rejection to be reviewed consist of:

**Ground 1.** Rejection of claims 10, 18, and 28 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

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<sup>4</sup> 31. A method of manufacturing an implantable medical device, comprising:  
purifying a polymer by:  
introducing the polymer into a mixing apparatus, the polymer having an impurity;  
introducing a first fluid into the mixing apparatus, the first fluid acting as a solvent for the impurity;  
mixing the first fluid with the polymer;  
removing at least a volume of the first fluid from the mixing apparatus such that the impurity is at least partially removed with the first fluid;  
introducing a second fluid into the mixing apparatus, the second fluid acting as a non-solvent for the impurity;  
mixing the second fluid with the polymer;  
removing at least a volume of the second fluid from the mixing apparatus such that the impurity is at least partially removed with the second fluid; and  
collecting the polymer after removal of the impurity; and  
coating an implantable medical device with the collected polymer, or fabricating the implantable medical device with the collected polymer, wherein the second fluid is not the same as the first fluid.

**Ground 2.** Rejection of claims 1, 3-5, 8-10, 31-33 and 35 under 35 U.S.C. 103(a) as being unpatentable over Buchanan et al. (U.S. Publication No. 2004/0063663) (hereinafter “Buchanan”) in view of Inoue et al. (U.S. Patent No. 5,762,944) (hereinafter “Inoue”), Hughes et al. (U.S. Patent No. 5,756,659) (hereinafter “Hughes”) and Goodson et al. (U.S. Patent No. 4,117,714) (hereinafter “Goodson”).

**Ground 3.** Rejection of claims 13, 16-18, 36, and 37 under 35 U.S.C. 103(a) over Buchanan, Inoue, Hughes, Goodson, and further in view of Berg et al. (EP 0623354) (hereinafter “Berg”).

**Ground 4.** Rejection of claims 23-29 under 35 U.S.C. 103(a) over Buchanan, Inoue, Hughes, Goodson, and further in view of Ainpour (U.S. Patent No. 4,526,579) (hereinafter “Ainpour”).

**Ground 5.** Rejection of claims 31-34 under U.S.C. 103(a) over Buchanan, Inoue, Hughes, Goodson, and further in view of Chudzik et al. (U.S. Patent No. 6,156,345) (hereinafter “Chudzik”).

## **VII. ARGUMENTS**

**Ground 1: Rejection of dependent claims 10, 18, and 28 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is improper and Appellants respectfully request reversal of the rejection.**

Claims 10 and 18 recite specific examples of fluids (water, isopropyl alcohol, methanol, FLUX REMOVER AMS, acetone, ethanol, dimethyl acetamide, acetonitrile, dimethyl formamide, cyclohexane, and dimethyl sulfoxide) that may be used to physically entrap, without dissolving, the impurity of independent claims 1 and 13, respectively. Claim 28 recites that the fluid of independent claim 23 (FLUX REMOVER AMS, dimethyl acetamide, dimethyl formamide, and dimethyl sulfoxide) is of a type to physically entrap the impurity without dissolving the impurity.

The issue under dispute is whether the specification has adequately, to one skilled in the art, designated these listed fluids as those that physically entrap an impurity without dissolving the impurity.

The Examiner has stated on page 2 of the Final Office Action that the claims fail to comply with the written description requirement since the “claim(s) contain subject

matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claim invention.” Then, the Examiner concluded that “[t]he fluids are generally listed in the specification without indication as to whether the Applicant had intended them to be used for dissolving or entrapping. Thus, the claims present new matter.”

The fundamental inquiry for a rejection of lack of written description is whether the specification conveys with reasonable clarity to those skilled in the art that applicant has position of the invention sought. *Vas-Cath, Inc. v. Mahurka*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). The lack of designating the recited fluids as a solvent or non-solvent for the impurity is not lacking support for written description when the specification as a whole is considered. More concretely, Appellants describe, on page 8 of the specification, the procedure for choosing different fluids, either solvents or non-solvents, for extracting the impurity. Definitions of “solvent” and “non-solvent” are provided on page 8 of the specification: “Solvent” is defined as “a substance capable of dissolving or dispersing one or more other substances or capable of at least partially dissolving or dispersing the substance(s) to form a uniformly dispersed mixture at the molecular- or ionic-size level. The solvent should be capable of dissolving at least 0.1 mg of the impurity in 1 ml of the solvent, and more narrowly 0.5 mg in 1 ml at ambient temperature and ambient pressure” (specification, page 8, lines 14-18). “Non-solvent” is defined as “a substance incapable of dissolving the other substance. The non-solvent should be capable of dissolving only less than 0.1 mg of the impurity in 1 ml of the non-solvent at ambient temperature and pressure, and more narrowly only less than 0.05 mg in 1 ml at ambient temperature and pressure” (specification, page 8, line 20, to page 9, line 2). In the very next paragraph, on page 9, the specification provides for specific examples of first and second fluids, which include those listed in claims 10, 18 and 28. Table 10 provides vapor pressure and boiling point of the fluids.

One with the most basic understanding of chemistry can appreciate that the type of impurity targeted is the determining factor for whether the fluid can be designated as a “solvent” or “non-solvent” based on the criteria enumerate on page 8. In other words, the list of fluids cannot be classified specifically as those that will only “dissolve” or only

“entrap” the impurities, since such categorization would be based on the impurity targeted. Additionally, the same fluid may be a “solvent” and a “non-solvent” depending on the impurity. Stated another way, Fluid A could be a solvent for impurity X, but a non-solvent for impurity Y. Based on the definitions and criteria enumerated in the specification, one of skill in the art would not only be able to easily comprehend whether a fluid is a solvent or non-solvent, but also be able to select a particular fluid for a particular impurity.

Therefore, Appellants have reasonably conveyed to one skilled in the relevant art that they had possession of the subject matter of claims 10, 18, and 28.

For the above reasons, Appellants submit that the rejection of claims 10, 18, and 28 under 35 U.S.C. § 112, first paragraph, is in error, and respectfully request that the rejection be reversed.

**Grounds 2, 3, 4 and 5: Rejections of claim 1, 3-5, 8-10, 13, 16-18, 23-29, and 31-37 under 35 U.S.C 103(a) over the combination of Buchanan, Inoue, Hughes, Goodson, Berg, Ainpour, and Chudzik are improper and Appellants request reversal of the rejections.**

Grounds 2, 3, 4 and 5 of this appeal include Examiner’s combination of Buchanan, Inoue, Hughes and Goodson as the common foundation for the rejections. More precisely, Buchanan and Hughes form the thrust or heart of the rejection with Inoue and Goodson providing the background. Berg, Ainpour and Chudzik are the third tier references, and merely fulfill some missing elements. Ground 3 is supplemented by the addition of Berg for the proposition that a polymer can be combined with a solvent to coat a stent. Ground 4 is supplemented by the addition of Ainpour for the proposition that it was known in the art to use dimethyl sulfoxide or dimethyl formamide for removal of residual monomers from a polymer. Ground 5 is supplemented by Chudzik for the proposition that poly(butyl methacrylate) can be used as a drug deliver polymer for medical devices.

Appellants’ position is simple, that the references which form the foundation of all rejections in Grounds 2-5 -- namely, Buchanan and Hughes, are impermissibly combined, in light of *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 417, 82



USPQ2d 1385, 1396 (2007) (“KSR”). Further, Appellants contend that Examiner’s position with respect to Goodson is in error. Since Buchanan and Hughes cannot be combined, and since Goodson does not fulfill the missing elements of Buchanan and Hughes, all rejections should fall, like a house of cards, and be reversed.

The Examiner’s position, as recited on pages 2-4 of the Final Office Action, can be accurately summarized as follows: Buchanan discloses a carrier polymer for coating stents. The carrier polymer with additives is added to a twin extruder. Buchanan is silent on introducing a fluid into the extruder and removing the fluid to remove impurities. Inoue recognizes the need to wash the polymer to remove impurities, such as unreacted monomer, in making medical devices such as stents. Hughes teaches a method of removing impurities, such as unreacted monomers, from a molten polymer inside a twin-screw extruder. The Examiner concludes that “[i]t would have been obvious to one of ordinary skill in the art at the time of invention to have introduced a fluid into the extruder to have removed impurities from the polymer of Buchanan because Inoue recognizes the need to remove impurities in a method of making a material for a medical device and because Hughes teaches that such an in-situ process is suitable in the art of removing impurities from a polymer.”

Since the combination of the three references fails to teach that the fluid is of the type of physically entrap the impurity without dissolving the impurity, the Examiner introduces a fourth reference into the equation, Goodson. The Examiner’s reliance on Goodson is best described in the own words of the Examiner, that “Goodson teaches that there are only a finite number of identified, predictable potential solutions in the method of removing impurities” including dissolving or entrapping impurities in a fluid.

Buchanan teaches a method of delivering a “guest molecule” by forming an “inclusion” complex” with a “host” molecule of acrylated cyclodextran [0043]. In one embodiment, a precipitation method, with the use of a common solvent, is performed to bind the guest to the host [0048]. Examples of the solvent include acetone, acetic acid, etc. [0048]. The host-guest inclusion complex are then combined with a carrier polymer by melt compounding into an extruder [0051]. Additives can also be added to the extruder [0051]. Moreover, Buchanan discloses a second alternative method, wherein the

guest, host, additive, and carrier polymer are added to an extruder for in-situ formation of the guest-host inclusion complex [0053].

Hughes is directed at improving the oxidative thermal stability of ethylene polymers by removing unreacted monomers, solvents and thermally unstable species. (Abstract). One or several stripping agents are introduced into an extruder. Examples of stripping agents disclosed include ethylene (col. 2, line 43) as well as metal hydroxides (e.g., sodium hydroxide or potassium hydroxide), nitrogenous bases (e.g., ammonium hydroxide) or water-soluble strong base organic amines (e.g., mono- di- and tri-methyl amines). (col. 5, lines 36-44). Hughes also discloses use of light hydrocarbons (e.g., ethylene, propylene or isobutane), water, aqueous solutions of metal hydroxides, steam, alcohol, carbon dioxide and/or nitrogen. (col. 6 line 67 to col. 7, line 5).

Again, Appellants' position is simple and very straight forward. Appellants respectfully submit that the basis for obviousness is erroneous since the combination (1) produces a grossly unpredictable result and (2) may render the primary reference, Buchanan, unsatisfactory for its intended purpose.

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. *KSR*

The combination of Buchanan with Hughes is tortuously unpredictable for two reasons. First, the addition of the Hughes' stripping agent may split the host-guest inclusion complex of Buchanan. In the first method of Buchanan, the host-guest are combined by addition of a common solvent to make the complex prior to adding the complex to the carrier polymer in the extruder [0048]. With respect to the parameters of the extruder, Buchanan emphasizes that care should be taken to prevent the guest from releasing from the host (see, for e.g., [0051] and [0053]). It is crucially important for the invention of Buchanan to keep the drug intact within the acylated cyclodextrin so as to provide for improved drug loading and release [0057]. It is reasonably predictable, or perhaps it can be said that it is grossly unpredictable at best, that the addition of the Hughes' stripping agents may cause the guest to separate from the host.

As for the second extrusion method where the guest and host are to be combined in-situ after adding to the extruder, Appellants respectfully submit that the addition of the

Hughes' stripping agent may interfere with the formation of the complex and addition of Hughes' stripping agent produces a highly unpredictable result.

Second, the stripping agents of Hughes are emphatically intended to remove unreacted monomers, solvents, and unstable species from the polymer. Appellants' position is that the addition of the Hughes' stripping agent to the extruder of Buchanan may result in the removal of the guest, host, guest-host complex and/or additives from the polymeric carrier. To repeat or reiterate, Buchanan adds the host-guest complex to the extruder to be compounded with the polymer carrier. In the alternative method, the host and guest are added to the extruder to be conjoined, in-situ, and compounded with the polymer carrier. In both methods, The Examiner has failed to recognize how addition of the Hughes' harsh caustic agents to the extruder of Buchanan may lead to removal of such materials from the extruder.

Moreover, if the combination of the references would render the reference inoperable or unsatisfactory for its intended use, a *prima facie* rejection for obviousness cannot be maintained. More specifically, if proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

Hughes teaches use of very harsh and highly toxic stripping agents such as sodium hydroxide, potassium hydroxide, ammonium hydroxide, and mono-/di-/tri-amines which will completely destroy the drug, rendering the invention of Buchanan inoperative and unsatisfactory for its intended purpose. Further, one skilled in the art would be gravely concerned about residual sodium hydroxide, potassium hydroxide, etc. remaining in Buchanan's carrier polymer, which would have an adverse impact on a patient. The stripping agents of Hughes have toxic qualities which are dangerous for medical device application. One skilled in the art would not look at using sodium hydroxide and potassium hydroxide in processing implantable medical devices such as stents.

Based on the high degree of uncertainty and the fact that Hughes would render Buchanan unsatisfactory for its intended use, one skilled in the art would not look to combine the stripping agents of Hughes to the extruder of Buchanan.

It is also worth noting that in constructing an obviousness position, references must be considered in their entirety or as a whole, including portions that would lead away from their combination. *In re Grasselli*, 713 F.2d. 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). First, Hughes teaches that an object of their invention is to remove “thermally unstable species.” (col. 3, line 6-7). Buchanan teaches that “processing temperatures should be less than that at which the guest molecule is released from the host acylated cyclodextrin [0051] (see also, [0053]). Thus, according to Buchanan, the inclusion complex is thermally sensitive. One skilled in the art would not look to combine a reference, Hughes, that emphatically teaches that it is an object to remove thermally unstable species with a reference, Buchanan, that emphatically teaches that it is critical to preserve and not disturb thermally unstable species by the process parameters used. These two teachings of Hughes and Buchanan run afoul to one another.

Second, Hughes teaches processing temperatures from 112 °C to 240 °C. (Table 6, col. 10). Most of the temperature of extruder zones of Hughes’ Table 6 are drawn to 200 °C and higher. Only one single zone is designated at a temperature of 112 °C. In other words, most of the length of the extruder is operated at a temperature of 200 °C and higher but for a sub-segment which operates at a temperature of 112 °C. Additionally, Tables 1 and 2 on col. 8 of Hughes all include extruder zone temperatures of 210 and 220 °C along the length of the extruder. Buchanan specifically states that “[p]referably, the process temperatures should be less than that at which the guest molecule is released from the host acylated cyclodextrin. That is, from about 100 deg. C to about 200 deg. C” [0051] (see also [0053]). It is the Appellants’ position that since Hughes teaches temperature zones in excess of 200 °C, one skilled in the art is guided away from making the combination with Buchanan, which teaches much cooler extruder temperatures. One cannot simply take the temperature of a single zone of 112 °C across the length of the extruder and ignore the fact that the remaining zone temperatures of Hughes would destroy the Buchanan host-guest complex.

Even with the title wave of KSR behind expansion of the scope of obviousness, Appellants respectfully submit that Buchanan simply cannot be combined with Hughes.

Finally, the Examiner's combination of Buchanan, Hughes and Inoue further fails, irrespective of the above-arguments, since the addition of Goodson does not fulfill the missing elements of Buchanan, Hughes, and Inoue. Goodson teaches that impurities may be removed from air by passing air through a film of water. Goodson states that the impurities can be "dissolved or entrapped" in the water (col 3. lines 39-42) (emphasis added). Appellants submit that Goodson -- as well as Buchanan Hughes, and Inoue -- fail to teach physically entrapping the impurity without dissolving the impurity as recited by claims 1, 13, and 28 (emphasis added). Goodson -- as well as Buchanan, Hughes and Inoue -- fail to teach that the fluid acts as a non-solvent for the impurity, as recited by claim 31 (emphasis added). Further, with respect to claim 31, the combination of the references fails to teach the use of both a solvent and a non-solvent (the solvent being different than the non-solvent). None of the references recognizes a distinction between using a solvent and a non-solvent and none teach or suggest the desirability of using a combination of a solvent and a non-solvent. In short, the combination of all references disclosed by the Examiner fails to teach these limitations of claims 1, 13, 28 and 31.

In curing this deficiency of Goodson, the Examiner grossly exaggerates the teachings of Goodson in supporting the proposition that there are only a finite number of predictable solutions for removing impurities, therefore it is obvious to use the one that has been claimed. At most, Goodson teaches that air impurities can be removed by passing air through water. It is an impermissible stretch to say that this statement generally teaches that there are a finite number of predictable solutions in removing impurities. A quick Google search reveals numerous ways to remove impurities using conventional and unconventional means such as, without limitation, CO<sub>2</sub> extraction, using enzymes, using bacteria, using plants, settling techniques, electrochemical purification techniques, filtration, chromatography, distillation, catalytic distillation, reverse osmosis, etc. Accordingly, the Examiner's proposition that there is a finite number of identifiable and predictable solutions in removing impurities is without merit. There is a finite number of identifiable and predicable solutions only if hindsight is used.

As indicated previously, Inoue, Berg, Ainpour and Chudzik do not cure any of the previously described deficiencies of making the combination of Buchanan and Hughes. Moreover, Goodson has been expanded well beyond its teachings. Goodson does not fulfill the missing elements in the claims as proclaimed by the Examiner. Applicants earnestly believe that since the combination cannot be made and since all limitations are not taught, the claims are patentable over the cited references. Reversal of all rejections is respectfully solicited.

## CONCLUSION

For all of the foregoing reasons it is submitted that all of the Examiner's rejections of claims 1, 3-5, 8-10, 13, 16-18, 23-29, and 31-37 are in error, and reversal of the Examiner's rejections and allowance of the application are respectfully requested.

**The Commissioner is hereby authorized to charge Deposit Account No. 07-1850 for any fees due.**

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## **VIII. Claims Appendix**



1. A method of manufacturing an implantable medical device, comprising:  
purifying a polymer by:  
introducing the polymer into a mixing apparatus;  
introducing a fluid into the mixing apparatus;  
mixing the fluid with the polymer;  
removing at least a volume of the fluid from the mixing apparatus such that an impurity is completely or at least partially removed with the fluid; and  
collecting the polymer after removal of the impurity; and  
coating an implantable medical device with the purified polymer, or fabricating the implantable medical device with the purified polymer;  
wherein the fluid is of a type to physically entrap the impurity without dissolving the impurity.
3. The method of Claim 1, wherein the mixing apparatus is selected from the group consisting of a single screw extruder, an intermeshing co-rotating extruder and a counter-rotating twin-screw extruder.
4. The method of Claim 1, wherein the polymer is exposed to a temperature equal to or greater than the melting temperature of the polymer.
5. The method of Claim 1, further comprising heating the polymer to a temperature equal to or greater than the melting temperature of the polymer.
8. The method of Claim 1, the method further comprising introducing a second fluid into the mixing apparatus, and mixing the second fluid with the polymer and removing the second fluid and an impurity from the mixing apparatus.

9. The method of Claim 1, wherein the polymer is selected from the group consisting of an ethylene vinyl alcohol copolymer, poly(butyl methacrylate), poly(vinylidene fluoride-co-hexafluoropropene), polyvinylidene fluoride, poly(L-lactic acid), poly(caprolactone), an ethylene-vinyl acetate copolymer and polyethylene glycol.
10. The method of Claim 1, wherein the fluid is selected from the group consisting of water, isopropyl alcohol, methanol, FLUX REMOVER AMS, acetone, ethanol, dimethyl acetamide, acetonitrile, dimethyl formamide, cyclohexane, dimethyl sulfoxide, and combinations thereof.
13. A method of manufacturing a coating for an implantable medical device, comprising:
- (a) purifying a thermoplastic polymer, the purifying including introducing the polymer into an extruder, introducing a fluid into the extruder, mixing the fluid with the polymer, removing at least a portion of the fluid and an impurity from the extruder, and collecting the polymer after removal of the impurity; and
  - (b) applying a composition to an implantable medical device, the composition including the purified polymer, a solvent and optionally a therapeutic agent; wherein the fluid is of a type to physically entrap the impurity without dissolving the impurity.
16. The method of Claim 13, the method further comprising exposing the polymer to a temperature equal to or greater than the melting temperature of the polymer while the polymer is in the extruder.

17. The method of Claim 13, wherein the polymer is selected from the group consisting of an ethylene vinyl alcohol copolymer, poly(butyl methacrylate), poly(vinylidene fluoride-co-hexafluoropropene), polyvinylidene fluoride, poly(L-lactic acid), poly(caprolactone), an ethylene-vinyl acetate copolymer and polyethylene glycol.
18. The method of Claim 13, wherein the fluid is selected from the group consisting of water, isopropyl alcohol, methanol, FLUX REMOVER AMS, acetone, ethanol, dimethyl acetamide, acetonitrile, dimethyl formamide, cyclohexane, dimethyl sulfoxide, and combinations thereof.
23. A method of manufacturing an implantable medical device, comprising:  
purifying a polymer by:  
introducing the polymer into a mixing apparatus;  
introducing a fluid into the mixing apparatus, the fluid selected from the group consisting of FLUX REMOVER AMS, dimethyl acetamide, dimethyl formamide, dimethyl sulfoxide, and combinations thereof;  
mixing the fluid with the polymer;  
removing at least a volume of the fluid from the mixing apparatus such that an impurity is completely or at least partially removed with the fluid; and  
collecting the polymer after removal of the impurity; and  
coating an implantable medical device with the purified polymer.
24. The method of Claim 23, further comprising exposing the fluid to a temperature equal to or greater than the boiling temperature of the fluid at ambient pressure after the fluid has removed the impurity.

25. The method of Claim 23, wherein the mixing apparatus is selected from the group consisting of a single screw extruder, an intermeshing co-rotating extruder and a counter-rotating twin-screw extruder.
26. The method of Claim 23, wherein the polymer is exposed to a temperature equal to or greater than the melting temperature of the polymer.
27. The method of Claim 23, further comprising heating the polymer to a temperature equal to or greater than the melting temperature of the polymer.
28. The method of claim 23, wherein the fluid is of a type to physically entrap the impurity without dissolving the impurity.
29. The method of Claim 23, the method further comprising introducing a second fluid into the mixing apparatus, and mixing the second fluid with the polymer and removing the second fluid and an impurity from the mixing apparatus.
31. A method of manufacturing an implantable medical device, comprising:  
purifying a polymer by:  
introducing the polymer into a mixing apparatus, the polymer having an impurity;  
introducing a first fluid into the mixing apparatus, the first fluid acting as a solvent for the impurity;  
mixing the first fluid with the polymer;  
removing at least a volume of the first fluid from the mixing apparatus such that the impurity is at least partially removed with the first fluid;  
introducing a second fluid into the mixing apparatus, the second fluid acting as a non-solvent for the impurity;  
mixing the second fluid with the polymer;

removing at least a volume of the second fluid from the mixing apparatus such that the impurity is at least partially removed with the second fluid; and  
collecting the polymer after removal of the impurity; and  
coating an implantable medical device with the collected polymer, or fabricating the implantable medical device with the collected polymer, wherein the second fluid is not the same as the first fluid.

32. The method of Claim 31, wherein after the first fluid has removed the impurity, exposing the first fluid to a temperature equal to or greater than the boiling temperature of the first fluid at ambient pressure prior to removing the first fluid from the mixing apparatus.

33. The method of Claim 31, wherein after the second fluid has removed the impurity, exposing the second fluid to a temperature equal to or greater than the boiling temperature of the second fluid at ambient pressure prior to removing the second fluid from the mixing apparatus.

34. The method of claim 31, wherein the polymer is poly(vinylidene fluoride-co-hexafluoropropene) or poly(butyl methacrylate).

35. The method of claim 1, further comprising exposing the fluid to a temperature equal to or greater than the boiling temperature of the fluid at ambient pressure prior to removing the fluid from the mixing apparatus.

36. The method of Claim 13, wherein the purifying further includes introducing a second fluid into the mixing apparatus, and mixing the second fluid with the polymer and removing the second fluid and the impurity from the mixing apparatus, wherein the

second fluid is of a type that dissolves the impurity and the second fluid is not the same as the first fluid.

37. The method of Claim 13, further comprising exposing the fluid to a temperature equal to or greater than the boiling temperature of the fluid at ambient pressure prior to removing the fluid.

## **IX. Evidence Appendix**

None.

**X. Related Proceedings Appendix**

None.